REMARKS

Claims 1, 3-5, 10-11, 13-15, 21, 25 and 26 are pending. By this Amendment, claim 26 is cancelled and claim 1 is amended.

Claim 1 was amended to incorporate the limitation of claim 26 "wherein the component A binds to a . . . cytokine receptor, hormone receptor, or growth factor receptor . . ." while also eliminating some of the other alternatives of claim 26.

Rejection of claims 1, 3, 4-5, 10-11, 13-14, and 21-26 for lack of possession.

The claims stand rejected under 35 U.S.C. §112¶1 for a lack of written description. The Office Action argues that there is a lack of possession of the claimed genera. The claimed genera are component A and component B. The amended claims provide for component A to be antibodies or the like that bind a limited set of receptor types. The Office Action admits that the "specification reasonably conveys antibodies as component A". Plainly, since the claimed antibodies are adequately described, the antibody derivatives, antibody fragments, and scFv are adequately described. Evidence is introduced into the record and is discussed with respect to enablement, below, that demonstrates that the claimed binding peptides are also adequately described. Accordingly, there are no reasonable concerns about possession of component A.

Component B is limited to DAPk and DAPK2 in the claims. The Office Action admits that DAPk is possessed for component B. There is no reasonable doubt that DAPk and DAPK2 are taught or can be practiced and the artisan certainly understands the scope of these terms so that the possession of component B is assured. The Office Action alleges that there are an unreasonable number of species for component B but there is no specific reasoning or argument in the Office Action explaining why DAPK2 is not possessed. There is no evidence that shows a lack of possession of DAPK2 or why there would be too many

species. Breadth is not indefiniteness, nor is it a lack of possession. What is missing in the Office Action's rationale is cogent reasons as to the reason that DAPK2 would not be possessed when DAPk is plainly possessed. Accordingly, there are no reasonable concerns about possession of component B.

The Office Action further expresses concerns about "S" as in dependent claim 13. The Office Action implies that the possibilities for "S" are overwhelming when combined with "A" and "B" so that all of the claims are rejected But this argument is legal error because an alleged lack of written description of claim 13 is not a basis for rejection of claim 1 or the other claims. Claim 1 is an open-ended claim that provides for the addition of other components, be they "S" or something else. The open-ended nature of claims language can not reasonably be used to argue that there are simply too many combinations of elements. Again, and very respectfully, there is no specific reasoning that explains why the particular "S" components are not possessed.

The crux of the Patent Office's arguments is that there are so many potential species that the genera can not possibly be adequately described. But the Patent Office is falling into an error of law, and there is clear precedent contrary to the Patent Office's position.

The Examiner has cited to the Federal Register that uses language taken from *Eli Lilly*, as per footnote 54 in column 3 of page 1106 of Federal Register Vol. 66, No. 4, January 5, 2001. In *Eli Lilly*, for claims to a genus of genetic materials, the Federal Circuit held that "a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function." University of California v. Eli Lilly & Co., 119 F.3d 1559, 1568 (Fed. Cir. 1997). Instead, the written description must define the genus to allow one skilled in the art to "visualize or recognize the identity of the members of the genus," e.g., by describing

a representative number of species or a description of "structural features commonly possessed by members of the genus that distinguish them from others." Eli Lilly, 119 F.3d at 1568.

Later cases, however, have held that a protein sequence does in fact place the artisan in possession of the encoding nucleic acid. In *Wallach*, the Court held that the state of the art has developed such that the complete amino acid sequence of a protein may put one in possession of its entire genus of DNA sequences. In re Wallach, 378 F.3d 1330, 1333 (Fed. Cir. 2004).

Wallach highlights a legal principle: *possession* is a measure of what the artisan understands when reading what is disclosed. In *Wallach*, the artisan is not told what the DNA "structure" is, but the artisan nonetheless possesses it because getting the structure is reasonably predictable. Thus *Wallach* is legally consistent with *Eli Lilly* but reaches a different result.

Capon discusses this principle in some detail: "It is well recognized that in the "unpredictable" fields of science, it is appropriate to recognize the variability in the science in determining the scope of the coverage to which the inventor is entitled. Such a decision usually focuses on the exemplification in the specification. [citations omitted] **Precedent illustrates that the determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter.** [citations omitted]. It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention. [citation omitted] While the Board is correct that a generic invention requires adequate support, the sufficiency of the support must be determined in the particular case." Capon v. Eshhar, 418 F.3d 1349, 1358-59 (Fed. Cir. 2005) (emphasis added).

In the instant case, it is respectfully submitted that getting an antibody or antibody derivative is just as predictable as getting a DNA sequence from a protein. In *Capon* and in the instant case, the lack of "structure" is not a concern because the artisan otherwise possesses the genus in a predictable manner. Indeed, in *Capon,* the issues revolved around a fusion protein that included a single chain antibody. Finding a suitable binding peptide is similarly possessed, for reasons discussed below.

Rejection of claims 1, 3, 4-5, 10-11, 13-14, and 21-26 for lack of enablement.

The Office Action has rejected the claims for lack of enablement. The rejection alleges a general lack of known structure and known function that provides a wide scope for the claims covering many embodiments.

In summary, the Office Action does not apply the appropriate legal test and errs in fact by arguing that the claims are directed to "any kinase" (Office Action page 6). As stated above, there are two components A and B. The component A is an antibody or a derivative, or a binding peptide. It is a well known fact that antibodies may be routinely generated for a protein such as a receptor as presently claimed. Similarly, binding structures that are synthetic peptides may be generated using routine techniques, as discussed below. Component B is directed to DAPk or DAPk2, which is a defined group of kinases that can be made and used as claimed in a routine manner. The Office Action's concerns about the group "S" in claim 13 are misplaced insofar as they are used to reject claim 1.

The first paragraph of 35 U.S.C. § 112 requires, *inter alia*, that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention without undue experimentation. In re Vaeck, 947 F.2d 488, 495 (Fed. Cir. 1991) (citing In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988)). Some experimentation, even a considerable amount, is not "undue" "if it is merely routine, or if the specification ... provides a

reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands, supra.* In particular, "sufficient disclosure ... to teach those of ordinary skill how to make and how to use the invention ... means that the disclosure must adequately guide the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility." In re Vaeck, 947 F.2d at 496.

The Patent Office falls into legal error when it makes general allegations that a there are too many embodiments or variables. The correct test is whether or not the claims can be practiced without undue experimentation. Application of Angstadt, 537 F.2d 498, 190 U.S.P.Q. 214 (C.C.P.A. 1976) examined a situation in an unpredictable art (chemical catalysis) wherein a limited number of examples were provided but the claims nonetheless read on an untold number of embodiments:

> "Appellants have apparently not disclosed every catalyst which will work; they have apparently not disclosed every catalyst which will not work. The question, then, is whether in an unpredictable art, section 112 requires disclosure of a test with every species covered by a claim. To require such a complete disclosure would apparently necessitate a patent application or applications with "thousands" of examples or the disclosure of "thousands" of catalysts along with information as to whether each exhibits catalytic behavior resulting in the production of hydroperoxides. More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid "literal" infringement of such claims by merely finding another analogous catalyst complex which could be used in "forming hydroperoxides." [¶ break omitted] The solicitor, without refutation by appellants, states: "Claim 27 literally reads on thousands of metal salt complexes in which the metal salt moiety may comprise any one of at least 50 metal cations combined with any inorganic anion." Application of Angstadt, 537 F.2d 498, 503-504.

The *Angstadt* court found for enablement when it considered that artisans could easily make the claimed variations of what was explicitly disclosed, even though there were very many such variations:

> "The process discovered by appellants is not complicated, and there is no indication that special equipment or unusual reaction conditions must be provided when practicing the invention. One skilled in this art would merely have to substitute the correct mass of a transition metal salt for the transition metal salts disclosed in appellants' 40 runs. Thus, we have no basis for concluding that persons skilled in this art, armed with the specification and its 40 working examples, would not easily be able to determine which catalyst complexes within the scope of the claims work to produce hydroperoxides and which do not. [¶ break omitted] Since appellants have supplied the list of catalysts and have taught how to make and how to use them, we believe that the experimentation required to determine which catalysts will produce hydroperoxides would not be undue and certainly would not "require ingenuity beyond that to be expected of one of ordinary skill in the art." Fields v. Conover, 443 F.2d 1386, 1390-91, 58 CCPA 1366, 1372, 170 USPQ 276, 279 (1971). " Application of Angstadt, 537 F.2d 498, 504.

The Patent Office implies that the skilled artisan can not understand how to effectively use the claimed A - B complex without undue experimentation. As stated above, however, the A component antibodies and binding ligands can be routinely generated. And the B component DAPk/DAPK2 kinases do not need to be discovered; they just need to be looked up in the electronic or journal literature.

Evidence is provided herein that the claimed peptidic binding ligands can be successfully using without undue experimentation. Several methods exist for selection of binding proteins or polypeptides such as phage display[a], yeast surface display[b], mRNA display[c] or peptide-on-bead display[d]. The cited references are: (a) Smith GP, Petrenko VA. Phage Display. Chem Rev 1997;97-2:391-410; (b) Boder ET, Wittrup KD. Yeast surface display for screening combinatorial polypeptide libraries. Nat Biotechnol 1997;15-6:553-7; (c) Xu L, Aha P, Gu K,

Kuimelis RG, Kurz M, Lam T, Lim AC, Liu H, Lohse PA, Sun L, Weng S, Wagner RW, Lipovsek D. Directed evolution of high-affinity antibody mimics using mRNA display. Chem Biol 2002;9-8:933-42; (d) Lam KS, Lebl M, Krchnak V. The "One-Bead-One-Compound" Combinatorial Library Method. Chem Rev 1997;97-2:411-48.

For instance, Lam et al. teach how to routinely screen literally millions of peptides, (e.g., 64 million, last paragraph of page 417) without undue experimentation, e.g., at section "B. Peptide libraries" staring at page 415. And Smith et al. teaches screening "billions" of peptides using processes accessible to an "ordinary researcher", page 407 last paragraph.

Rejection of claims 1, 3, 4-5, 10-11, 13-14, and 21-26 for obviousness

Claims 1, 3, 4-5, 10-11, 13-14, and 21-26 have been rejected under 35 U.S.C. §103(a) for obviousness over WO 2004/078215 or U.S. Pat. No. 7,419,811 (collectively Lavie et al.) in light of Shohat et al., Biochem Biophy Acta 2002, 1600:45-50.

Lavie et al. disclose binding CD33, a cell surface antigen that is not a receptor, so that this rejection is moot in light of the amended claims. The presently claimed invention is directed to cell surface receptors. Disclosure of CD33 or a cell surface antigen is not disclosure of the specifically claimed cell receptors. Shohat et al. does not make up for this defect. A *prima facie* case of obviousness requires disclosure of every claimed element. But the cited references do not disclose the receptors (cytokine, hormone or growth factor) as claimed in the context of the claims as a whole. Therefore there is no *prima facie* case of obviousness.

Request for Relief

In view of the foregoing, it is submitted that this application is in condition for allowance. Favorable consideration and prompt allowance of the application are respectfully requested.

The Examiner is invited to telephone the undersigned if the Examiner believes it would be useful to advance prosecution.

Respectfully submitted,

/Curtis B. Herbert/
Curtis B. Herbert, Ph.D., Reg. #45,443

Customer No. 62274
Dardi & Herbert, PLLC
Moore Lake Plaza, Suite 205
1250 East Moore Lake Drive
Fridley, Minnesota 55432
Telephone: (763) 412-3824